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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,611	07/22/2002	Martin Von Bergen	029976-0101	9060

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EXAMINER

CHEU, CHANGHWA J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 12/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/070,611

Applicant(s)

BERGEN ET AL.

Examiner

Jacob Cheu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 October 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 28-54 is/are pending in the application.
- 4a) Of the above claim(s) 30-32, 42-46, 52 and 53 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 28, 29, 33-41, 47-51 and 54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I, claims 28-29, 33-41, 47-54 and SEQ ID No. 9 on 10/12/2004 is acknowledged. The traversal is on the ground(s) that the Group I, II and III form a single inventive concept, and further search would not impose undue burden to the examiner. This is not found persuasive because examiner had shown a prior art (WO 96/30766, now US 6376205) teaches the recited method, therefore the instant invention group I does not fulfill the requirement of unity under Rule 13.1 PCT, and further search required for the examination.

The requirement is still deemed proper and is therefore made FINAL.

Applicant elects SEQ ID No. 9 for examination. Accordingly, claims 52-53 using SEQ ID No. 7 or 8 other than SEQ ID No. 9, will not be examined.

Currently, claims 28-29, 33-41, 47-51, 54 are under examination. Claims 30-32, 42-46, 52-53 are withdrawn from further consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement

2. Claims 28-29, 33-41, 47-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the full lengths of SEQ ID No. 6, 7, 8 and 9, does not reasonably provide enablement for the corresponding fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Fragment

Regarding fragments of SEQ ID: 6, 7, 8, and 9 polypeptides, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry 29(37): 8509-8517; "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research 10:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel

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applications of computational approaches in the genomic era.” Trends in Biotech. **18**(1): 34-39, especially p. 36 at Box 2;” Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) “The challenges of genome sequence annotation or ‘The devil is in the details’.” Nature Biotechnology **15**:1222-1223; Brenner (April 1999) “Errors in genome annotation.” Trends in Genetics **15**(4): 132-133;)

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 28-29, 33-41, 47-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 28, it is not clear whether the recited method requires fluorescence or radiolabeled materials for conduction the assay to determine the assembly of PHF. Particularly, applicant indicates using fluorimetric method in determining PHF assembly in the specification (See Figure 2).

With respect to claim 28, step (a), line 2, “fragment(s) thereof” is vague and indefinite. It is not clear about the metes and bounds of the recited polypeptides.

With respect to claim 29, line 3, “protein fragments” is vague and indefinite. It is not clear about the metes and bounds of the ‘protein fragments’

With respect to claim 33, it is not complete for the recited method to prepare the said inhibitor. It is not clear what steps(s) is needed to synthesize the inhibitor, i.e. organic synthesis or polypeptide synthesis.

With respect to claim 41, it is not clear applicant intention whether the suitable means of detection is needed since applicant recites “optionally.”

With respect to claim 41, it is not clear what constitutes “suitable means of detection”.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 28-29, 33-41, 49-51, 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Wischik et al. (WO 96/30766).

Wischik et al. teach a method for identifying and obtaining an inhibitor capable of modifying the paired helical filaments (PHF) formation. Wischik et al. teach incubating a tau protein or its derivative peptide, i.e. SEQ ID No. 1 (comprising the instant elected SEQ ID No. 9) with a compound suspected of being capable of inhibiting the tau-tau association, e.g. PHF assembly, and detect the increase or decrease of the assembly of PHF as indicative of inhibitor of PHF formation. (See page 8, line 12-26; SEQ ID No. 1, Figures 6).

With respect to claim 34, Wischik et al. teach immobilizing peptide(s) on a solid phase (See claim 3).

With respect to claim 35, Wischik et al. teach conducting the assay in a sodium chloride or salt or salt mixture condition (See claim 7).

With respect to claims 36-41, Wischik et al. teach that the tau protein can be recognized by monoclonal antibody at certain amino acid residues (page 6, line 11-25). The antibody can bind to the tau protein, comprising the SEQ ID No. 9. (See page 6, line 11-25). Wischik et al. teach that the tau-tau protein assembly inhibitor might be applicable for Alzheimer's disease (See page 1-2, Introduction).

With respect to claim 49-51 and 54, Wischik et al. teach using recombinant techniques to produce the tau peptide, i.e. SEQ ID No. 9, in E Coli cell culture system.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

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3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
7. Claims 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wischik et al. in view of Vandermeeren et al. (US 20030138972).

Wischik et al. reference teaches a method of identifying and obtaining an inhibitor capable of modifying the PHF formation by use of a peptide comprising SEQ ID No. 1(as recited SEQ ID No. 9 in instant invention) immobilizing on a solid support and incubating the SEQ ID No.1 peptide with potential compound(s) to determine its affect on the assembling of the PHF formation (See paragraph 4 in this Office Action). However, Wischik et al. do not explicitly teach using a kit to conduct the assay for screening potential candidates of PHF inhibitors. Vandermeeren et al. teach using a standard kit containing protein recognizing PHF-tau region as a convenient and economical tool for detecting neurological diseases (See section 0082, 0091, claim 15). Thus, one of ordinary skilled in the art at the time the invention was made would have been motivated to make a kit useful for the detection of an inhibitor capable of modifying the PHF formation because standard kits enhance the probability of the reproducibility and efficiency of the detection process.

Conclusion

8. No claim is allowed.

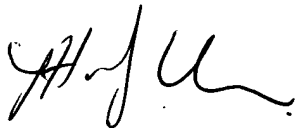
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 571-282-0814. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jacob Cheu
Examiner



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December 15, 2004



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12/26/04